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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/826,113

04/16/2004

Piotr Chomczynski

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EXAMINER

BABIC, CHRISTOPHER M

ART UNIT

PAPER NUMBER

1637

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/826,113	<b>Applicant(s)</b> CHOMCZYNSKI, PIOTR	
	<b>Examiner</b> CHRISTOPHER M. BABIC	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 29,30,39,41,44,46-52 and 59-63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 44,62 and 63 is/are allowed.
- 6) ☒ Claim(s) 29,30,39,41,46-52 and 59-61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/12/09</u> .   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Status of the Claims***

Claim(s) 29, 30, 41, 44, 46-52, and 59-63 are pending. The following Office Action is in response to Applicant's communication dated October 31, 2008.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on January 12, 2009 was filed after the mailing date of the NON-FINAL Office Action on March 18, 2008. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Claim Objections - Withdrawn***

Applicant cancelled claim 30 rendering the objection moot.

### ***Claim Rejections - 35 USC § 112 - Indefiniteness - Withdrawn***

Applicant's claim amendments are sufficient to overcome the rejection of claim(s) 50 presented in the Office Action dated March 18, 2008.

### ***Claim Rejections - 35 USC § 112 - Indefiniteness - New Grounds***

The following new grounds of rejection is made in view of a newly discovered indefiniteness within the claimed invention.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claim(s) 59-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The term "higher" in is a relative term which renders the claim indefinite. The term "higher" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

***Claim Rejections - 35 USC § 103 - Withdrawn***

Applicant's arguments are sufficient to overcome the rejection of claim(s) 47-51 over Chen and Chomczynski (see remarks pg. 15-17). Thus, the rejection has been withdrawn.

***Maintained Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claim(s) 29, 30, 39, 41, 46, 52, and 59-61 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (Chinese patent 1,220,995, translation provided) in view of Chomczynski (U.S. 5,346,994).**

With regard to claims 29 and 59, Chen teaches a method for isolating purified RNA from a biological sample of (see page 3, bottom half, for example or page 4) comprising: a) treating the sample comprising phenol at a final concentration ranging from about 10% w/w to about 60% w/w and at least one ribonuclease inhibitor (see page 6, where 12-46% phenol is used in conjunction with guanidine isothiocyanate, an RNase inhibitor and see page 8, preferred embodiment 2, step 1, where the phenol reagent with 30% w/w is added to the tissue), b) mixing the sample with at least one hydrophobic solvent and a buffer at a concentration sufficient to maintain a pH in the range from about pH 3.6 to below pH 4.0 (see page 8, preferred embodiment 2, where the pH of the phenol reagent is pH 3.5, which is about 3.6 and where the hydrophobic solvent chloroform/isoamyl alcohol is added to the solution. Further note that Chen teaches overlapping ranges of pH from 3.5 to 6.5 and the use of glacial acetic acid to regulate the pH value (see page 3)), c) recovering the purified RNA from an aqueous phase to which about an equal volume of a water soluble organic solvent is added to precipitate the purified RNA (See page 8, preferred embodiment 2, where the aqueous phase is precipitated with isopropanol), d) washing and solubilizing the precipitated

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RNA (see page 9, where the RNA precipitate is washed with alcohol and dissolved in a buffer).

With regard to claim 30, Chen teaches the use of acetate and citrate buffers (see page 8, preferred embodiment 2, lines 3 and 4).

With regard to claims 32-34, Chen teaches the use of ribonuclease inhibitors (see page 8, preferred embodiment 2, line 1, where the chaotropic salt guanidine isothiocyanate is used as an RNase inhibitor at a concentration in the range of 0.5 M to about 6M).

With regard to claims 35 and 36, Chen teaches the use of detergents such as SDS and sarcosine including a range of 0.1.% SDS (see page 8, preferred embodiment 2, lines 2-3).

With regard to claims 37-39, Chen teaches the use of sodium acetate and trisodium citrate (where claim 38 indicates that acetate is a preferred salt and claim 39 indicates that citrate is a preferred chelating agent).

With regard to claim 41, Chen teaches the use of guanidine salts (see page 8, line 1).

With regard to claims 46, Chen teaches a pH range of 3.5-6.5 and exemplifies a pH of 3.5 (see page 3 and see page 8, preferred embodiment 2).

With regard to claims 52, 60, and 61, Chen teaches precipitation with isopropanol (see page 8).

While Chen teaches the use of a pH adjusting component, Chen does not state that the amount used will be sufficient to maintain pH.

Chomczynski teaches the use of a pH adjusting component in an RNA solvent solution where "the solvent solution may include a buffering component, such as sodium acetate or sodium citrate, in an amount sufficient to maintain the pH of the solution (see column 3, lines 17-22)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen, who notes a desire to "regulate the pH value (see page 3)", to incorporate enough buffering component as taught by Chomczynski since Chomczynski notes "the solvent solution may include a buffering component, such as sodium acetate or sodium citrate, in an amount sufficient to maintain the pH of the solution (see column 3, lines 17-22)." An ordinary practitioner would have been motivated to include sufficient buffering in the isolation buffer of Chen in order to maintain the pH since both Chen and Chomczynski teach and motivate the use of buffering components to maintain the pH of the solution.

### **Response to Arguments**

Applicant's arguments have been fully considered but they are not persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

With regard to Applicant's arguments relating to the lack of motivation provided in Chomczynski, a skilled artisan would have recognized that the addition of buffering component in an amount sufficient to maintain the pH of the isolation solution would have avoided unwanted radical pH change during isolation.

Furthermore, as submitted previously, The current examiner of record has reviewed the 1/17/2008 declaration and agrees with the previous examiner that the declaration provides proof of unexpected results relative to Chen regarding the presence of DNA with respect to particular embodiments of a pH of 3.8, 40% phenol, 4M guanidine, 5% glycerol, 0.1% sarcosine, and 10mM sodium citrate. This example does not provide support that other conditions, such as pH 3.5, which must literally be within the scope of "about pH 3.6", if anything is, or other reagent conditions, will achieve the same results. Furthermore, one of Applicant's main arguments as to the reason for the unexpected results is that a "scaling agent" as in Chen's method, is not present in the concentration Chen uses. This is not a requirement of the claimed inventions. Thus, the claimed inventions are not commensurate in scope with the declaration. As MPEP 716.02(d) notes "the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support."

With regard to Applicant's arguments relating to claim 59, the claimed invention does not preclude the isolation of lower molecular weight RNA, i.e. the word "selectively" is not defined in such a manner so as to preclude the isolation of lower molecular weight RNA.



Thus, the rejection is maintained.

***Claim Rejections - 35 USC § 103 - New Grounds***

The text of those sections of Title 35, U.S. Code not included in this action can be found above.

**Claim(s) 47-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (Chinese patent 1,220,995, translation provided) in view of Chomczynski (U.S. 5,346,994), and in further view Focus (1998) 20(2):36.**

The teachings of the previously applied reference(s) have been outlined in the above rejections. The previously applied reference(s) do not expressly teach sedimenting the sample prior to the addition of the phase separation agent.

Focus teaches that an intermediate centrifugation step, prior to the addition of chloroform, will remove undesired polysaccharides and genomic DNA.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the isolation buffer of Chen to perform an intermediate sedimentation step prior to addition of chloroform since Focus notes in response to the problem in RNA isolation with Trizol reagent (a reagent similar to Chen's except for the pH) that "If my tissue has a high content of proteoglycans and/or polysaccharides, what can I do to ensure that these compounds don't contaminate the RNA? (see page 36)" and the Focus response is "Centrifuge following homogenization

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before adding chloroform at 12,000 x G at 4 C (see page 36)". An ordinary practitioner would have been motivated to perform this centrifugation since Focus notes that the centrifugation will "pellet polysaccharides (also pellets genomic DNA)", so that the centrifugation step will enhance the purity and separation of the RNA from contaminating genomic DNA, as desired by Chen.

### ***Conclusion***

**Claims 29, 30, 39, 41, 46-52, and 59-61 are rejected.**

**Claims 44, 62, and 63 are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christopher M. Babic/  
Patent Examiner  
Art Unit 1637  
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